IN THE CLAIMS:

Please cancel claims 5, 6, 8, 14-15, 17-20, 47 and 55-56. Please amend claims 1-3, 7, 12-13, 16, 21, 25-28, 33, 38, 40-41, 43-44, 46, 48-52, and 57-58 in accordance with 37 C.F.R. § 1.121(c)(1)(i), *i.e.*, the rewritten or newly added claims are in clean form without markings. Please add new claims 59-78. A separate document showing the changes, in accordance with 37 C.F.R. § 1.121(c)(1)(ii), is attached.

1. (Amended) A device for manipulating a molecule *in vivo* relative to a target tissue comprising a support and at least one electrode member extending away from and affixed to for defining the support, the at least one electrode member having at least one conductive portion, wherein:

the sum of electrode members and conductive portions equals at least three;

the conductive portions are separated by nonconductive portions, each conductive portion being in circuit communication with a respective portion of a source of electrical energy;

the conductive portions are configured to establish a first electromagnetic field between selected conductive portions sufficient to manipulate a molecule relative to a target tissue and a second electromagnetic field sufficient to cause transient permeability of a cell membrane within the target tissue; and

at least two of the conductive portions are locatable against a selected portion of the target tissue.

2. (Amended) The device recited in Claim 1, wherein the conductive portions and the nonconductive portions are located on the same electrode member.

3. (Amended) The device recited in Claim 1, wherein the conductive portions and nonconductive portions are located on separate electrode members.

7. (Amended) The device recited in Claim 1, wherein the support comprises a generally cylindrical post having a portal therethrough from a top end to a bottom end and the device further comprises:

a disc affixed to the post bottom end, the disc having a bottom surface having an outer downwardly depending annulus comprising alternating conductive portions separated by nonconductive portions, the electrode member comprising the annulus and the conductive portions serving as electrodes; and

a lead in circuit communication with each conductive portion extending from the disc through the post portal to the top end thereof.

12. (Amended) The device recited in Claim 7, wherein the disc comprises a section having sufficient transparency to permit visualization of the selected target tissue therethrough.

13. (Amended) The device recited in Claim 1, further comprising means for delivering a preselected pattern of signals to selected conductive portions to effect a desired molecular result.

16. (Amended) The device recited in Claim 1, the electrode member further comprising a downwardly depending post affixed adjacent a bottom end of the support, the post having at least one conductive portion on a surface thereof.

21. (Amended) The device recited in Claim 16, wherein the electrode member comprises a plurality of downwardly depending posts, each post axially movable between a first position and a second position lower than the first position and biased to the second position, for achieving contact between each post and a target tissue surface.

25. (Amended) The device recited in Claim 21, wherein each post has a pointed conductive bottom tip, the tips disposed at a radially inwardly facing angle to each other, each post inwardly movable between a first position and a second position wherein the tips are closer

together than in the first position, the second position for achieving contact with the target tissue between the tips.

26. (Amended) The device recited in Claim 1, further comprising a pair of electrode members movably affixed to the support in separation-adjustable fashion, each electrode member comprising means for affixing at least one conductive portion thereto, said conductive portions serving as electrodes.

27. (Amended) The device recited in Claim 26, wherein each electrode member comprises an insulating plate, and wherein a plurality of electrodes affixed to a surface of each plate, the plates configured to contact at least a portion of the target tissue therebetween.

28. (Amended) The device recited in Claim 1, further comprising means for establishing at least two substantially different voltages approximately simultaneously on two or more conductive portions.

33. (Amended) The device recited in Claim 1, further comprising means to facilitate contact between the electrode member and the target tissue.

38. (Amended) A method for achieving a desired distribution and delivery of one or more molecules from an initial location into a target tissue, the method comprising the steps of:

placing at least one electrode member comprising at least one conductive portion, wherein at least two conductive portions are generally adjacent, but in nonpenetrating fashion to, a surface adjacent a target tissue, each conductive portion in circuit communication with a respective portion of a source of electrical energy;

establishing a first electrical potential between at least two conductive portions sufficient to cause electromigration of the desired molecule from the initial location toward the target tissue; and

establishing a second electrical potential between at least two conductive portions sufficient to cause electroporation in the target tissue for enhancing a movement of the desired molecule into a cell thereof.

40. (Amended) The method recited in Claim 38, further comprising the step of establishing a third electrical potential between at least two conductive portions sufficient to cause electromigration of the desired molecule from a location adjacent the target tissue through a pore in a cell membrane of the target tissue into an interior thereof.

41. (Amended) The method recited in Claim 40, wherein the establishing step comprises establishing a series of third electrical potentials in a predetermined sequence of pulses.

43. (Amended) The method recited in Claim 38, wherein the electromigration is effected to cause the molecule to penetrate a skin layer.

44. (Amended) A method for delivering a bioactive molecule from an initial location to a target tissue, the method comprising the steps of:

placing at least one electrode member having conductive portions, wherein at least two conductive portions are against a surface generally adjacent, but in nonpenetrating fashion to, a target tissue, each conductive portion serving as an electrode and being in circuit communication with a respective portion of a source of electrical energy;

activating at least two electrodes to achieve an electromigration of the bioactive molecule from the initial location to a location adjacent the target tissue; and

activating at least two electrodes to achieve electroporation of a cell membrane within the target tissue sufficient to permit entry of the biological molecule into the cell interior.

46. (Amended) A method for bringing a first and a second molecule from two respective initial locations into apposition at a desired target tissue site for permitting a reaction therebetween, the method comprising the steps of:

placing at least one electrode member having conductive portions, wherein at least two conductive portions are against a surface generally adjacent, but in nonpenetrating fashion to, a target tissue, each conductive portion serving as an electrode and being in circuit communication with a respective portion of a source of electrical energy;

activating the conductive portions to cause an electromigration of the first molecule to a third area adjacent the target tissue site;

activating the conductive portions to cause an electromigration of the second molecule to a third area adjacent the target tissue site; and

permitting the first and the second molecule to react at the third area.

48. (Amended) The method recited in Claim 46, wherein the electromigration of the first molecule is effected to cause the first molecule to penetrate a skin layer.

49. (Amended) The method recited in Claim 46, wherein the activation steps cause the first and the second molecule to be delivered to the cytosol of cells comprising the target tissue.

50. (Amended) The method recited in Claims and 77, wherein the penetration step is effected through a biological tissue other than skin.

51. (Amended) The method recited in Claim 46, further comprising the step, prior to the activating step, of activating two conductive portions to cause electroporation in the target tissue.

52. (Amended) The method recited in Claim 46, further comprising the step, following the activating step, of activating two conductive portions to cause electroporation in the target tissue.

57. (Amended) A method for making a molecule electromanipulator comprising the steps of:

affixing at least one electrode member comprising conductive portions to a support in spaced-apart relation;

providing circuit communication between each conductive portion and a source of electrical energy, the conductive portions configured to establish a first electromagnetic field *in vivo* between selected conductive portions for manipulating a molecule relative to a target tissue and a second electromagnetic field *in vivo* for causing transient permeability of a cell membrane within the target tissue.

58. (Amended) The method recited in Claim 57, further comprising the step of providing means for controlling the switching means adapted to activate the conductive portions in a preselected pattern.

59. (New) The device recited in claim 7, wherein the disc has a noncircular shape.

60. (New) The device recited in Claim 7, wherein the post has a geometry that facilitates grasping the device for accessing the target tissue.

61. (New) The device recited in Claim 1, further comprising at least two generally rectangular, striplike electrode members, each striplike electrode member movable between a first position and a second position, wherein the electrode members are closer together than in the first position.

62. (New) The device recited in Claim 60, further comprising a first restraining means for selecting the minimum distance between electrode members, and a second restraining means for selecting the maximum distance between electrode members.

63. (New) The device recited in Claim 61, wherein the first restraining means comprises an insert positionable in the lumen between the electrode members.

64. (New) The device recited in Claim 61, wherein the first restraining means comprises a set screw.

65. (New) The device recited in Claim 61, wherein the second restraining means comprises a torodial ring.

66. (New) The device recited in Claim 60, further comprising a lead in circuit communication with each conductive portion adapted for electrical communication with the source of electrical energy.

67. (New) The method recited in Claim 43, wherein the penetration is effected through biological tissue other than skin.

68. (New) The method recited in Claim 38, wherein the establishment of the second electrical potential causes the molecule to be delivered to the cytosol of the cells that comprise the target tissue.

69. (New) The method recited in Claim 38, wherein the first potential causing electromigration is used independently of electroporation.

70. (New) The method recited in Claim 38, wherein the second potential causing electroporation is used independently of electromigration.

71. (New) The method recited in Claim 38, wherein the electroporation is caused prior to the electromigration.

72. (New) The method recited in Claim 45, wherein the penetration is effected through biological tissue other than the skin.

73. (New) The method recited in Claim 44, wherein the electroporation of the second electrical potential causes the molecule to be delivered to the cytosol of the cells that comprise the target tissue.

74. (New) The method recited in Claim 44, wherein electromigration is used independently of electroporation.

75. (New) The method recited in Claim 44, wherein electroporation is used independently of electromigration.

76. (New) The method recited in Claim 44, wherein the electroporation is caused prior to the electromigration.

77. (New) The method recited in Claim 46, wherein the electromigration of the second molecule is effected to cause the second molecule to penetrate a skin layer.

78. (New) The method recited in Claim 57, further comprising switching means between each conductive portion and the electrical energy source to permit activation of the conductive portions on each electrode member.

Very respectfully,
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